

WE CLAIM:

1. A system for delivering fluid to a sample holder comprising
a fluid source,
5 a pump connected to the fluid source,
a dispenser assembly having an orifice, and
a conduit path extending from the pump to the orifice of the dispenser assembly,
the conduit path remaining open and unconstricted between successive non-contact
deposition of fluid aliquots having a volume of less than about 5 microliters per aliquot.

10 2. The system of claim 1 further comprising a controller that determines the
volume of each fluid aliquot.

15 3. The system of claim 1, wherein the pump device pumps incrementally at a
rate corresponding to the rate of aliquot deposition.

4. The system of claim 1, wherein the dispenser assembly has a hydrophobic
tip portion.

20 5. The system of claim 4, wherein the tip portion is made of a heat-shrinkable
material.

6. The system of claim 5, wherein the tip portion is made of material selected from the group consisting of PTFE, polypropylene, polyethylene, and FEP.

7. The system of claim 1, wherein the dispenser assembly has a tip portion
5 made of sapphire.

8. The system of claim 1, wherein the orifice is formed at an end of a tube-like tip portion, the tip portion having a wall thickness around the orifice of less than about 8 thousandths of an inch.

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9. The system of claim 1, wherein the orifice has an inner diameter of less than about 200-microns.

10. The system of claim 1, wherein the pump is connected to the dispenser
15 assembly by a tube having a distal end, the tip portion having a flange on a proximal end, the distal end of the tube being held in contact with the flange of the tip portion.

11. The system of claim 1, wherein the pump is a syringe pump.

20 12. The system of claim 11, wherein the syringe pump has a linear motor.

13. The system of claim 11, wherein the pump has a stepper motor.

14. The system of claim 10, wherein the dispenser assembly includes a manifold for holding the distal end of the tube in contact with the flange of the tip portion.

5 15. The system of claim 14, wherein the same manifold secures connection of a plurality of tubes to respective tip portions to define an array of fluid dispensing channels.

10 16. The system of claim 15, wherein the array of fluid dispensing channels corresponds to an array of wells in a microplate.

15 17. The system of claim 15, wherein the array of fluid dispensing channels corresponds to an array of sites on a biochip.

18. The system of claim 15, wherein the array corresponds to wells in a standard 96-well microplate.

20 19. The system of claim 15 further comprising a sample holder registration mechanism that alters the position of a sample holder relative to the manifold so that the same array of fluid dispensing channels can be used to deposit fluid into sample holders having varying densities of deposition sites.

20. A fluid dispensing assembly comprising
a manifold device having a plurality of apertures,
a plurality of tip devices, each tip device having a conduit channel connected
contiguously with an aperture in the manifold, each tip device being made of a heat-
5 shrinkable hydrophobic material and having a wall thickness small enough so that
droplets of less than 5 microliters per droplet can be separated from the tip device without
contacting the droplets to a surface and without closing or constricting the conduit
channel.

10 21. The assembly of claim 20 further comprising a plurality of pumps, each
pump being connected to a tip device.

22. The assembly of claim 21, wherein the pumps are syringe pumps.

15 23. The assembly of claim 21, wherein each pump has a stepper motor.

24. The assembly of claim 21, wherein each pump has a linear motor.

25. The assembly of claim 20 further comprising a fluid source station having
20 one or more reservoirs, the pumps being connected to said one or more reservoirs.

26. The assembly of claim 25 further comprising an interchangeable conduit network allowing any combination of tip devices to be connected to any one of the reservoirs.

5 27. The assembly of claim 20, wherein each tip device has a circumferential wall defining an orifice, the wall having a thickness that is less than about 8 thousandths of an inch.

10 28. The system of claim 20, wherein each tip device is made of a hydrophobic material.

15 29. The system of claim 28, wherein each tip device is made of a material selected from the group consisting of PTFE, polypropylene, polyethylene, and FEP.

30. A fluid dispensing system comprising
an array of N dispense tips, each dispense tip being connected to a separate
syringe pump,
5 where X is in the range of 1 to N, and

a changeable fluid conduit network capable of permitting: (a) each pump to be
connected to a separate fluid reservoir, (b) each pump to be connected to the same fluid
reservoir, (c) any subset of pumps to be connected to the same fluid reservoir while one
or more other tips are connected to another fluid reservoir.

10 31. The system of claim 30, wherein the dispense tips are configured to
dispense droplets in a range of volumes including volumes of less than about 5
microliters per droplet without contacting the droplet to a surface.

15 32. The system of claim 31, wherein each dispense tip has a hydrophobic wall
defining an orifice having a diameter of less than about 200 microns, the wall having a
thickness of less than about 8 thousandths of an inch.

20 33. The system of claim 30, wherein the dispense tips are made of a material
selected from the group consisting of sapphire, PTFE, polypropylene, polyethylene, and
FEP.

34. The system of claim 30, wherein each pump includes a linear motor.

35. A device for dispensing fluid to a sample or sample holder, the device comprising

a fluid reservoir,

a pump device connected to the fluid reservoir, and

5 a dispense element operatively connected to the pump device, wherein the pump device drives fluid incrementally to the dispense element with sufficient velocity and acceleration so that a fluid aliquot of less than about five microliters separates from the dispense element without contacting a surface.

10 36. The device of claim 35, wherein the dispense element has a hydrophobic tip with a tube-like wall defining an orifice and is configured to reduce the affinity of dispensed fluid for the dispense element, so that dispensed fluid separates from the dispense element.

15 37. The device of claim 36, wherein the wall of the tip has a thickness of less than about 8 thousandths of an inch.

38. The device of claim 36, wherein the orifice has a diameter of less than about 200 microliters.

20 39. The device of claim 35, wherein the dispense element has a tip portion made of a material selected from the group consisting of PTFE, polypropylene, polyethylene, and FEP.

40. A method of dispensing fluid aliquots of less than about 1 microliter per
aliquot comprising
connecting a pump to a dispense tip via a conduit path,
pulsing fluid through the conduit path, and
5 ejecting a fluid aliquot of less than about 1 microliter from the dispense tip for
each fluid pulse.

41. The method of claim 40, wherein the ejecting step is carried out without
closing or constricting the conduit path.

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42. The method of claim 40 further comprising the step of
directing ejected fluid aliquots into wells of a microplate.

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43. The method of claim 40 further comprising the step of
directing ejected fluid aliquots to sites on a biochip.

44. The method of claim 40 further comprising the step of
minimizing interfacial attraction between the dispense tip and the fluid by using a
hydrophobic dispense tip, the dispense tip having a wall defining an orifice, the wall
20 having a thickness of less than about eight thousandths of an inch.

45. A fluid dispensing system comprising
a fixed two dimensional array of dispense tips that are capable of non-contact
deposition of fluid aliquots of less than about 5 microliters per aliquot simultaneously
into a plurality of rows of wells in a microplate.

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46. A fluid dispensing system comprising
a syringe pump having a linear motor, and
a dispense tip connected to the pump for depositing a fluid aliquot to a sample
holder.

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47. The system of claim 46, wherein the syringe pump has a linear stepper
motor.

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48. The system of claim 46, wherein the syringe pump has a linear servo motor.

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49. An integrated high throughput analysis system comprising
an assay preparation unit that combines reagents and samples in wells of a
microplate,
an analyzer integrated with the assay preparation unit, wherein the analyzer
20 includes optics that are substantially matched to the wells of the microplate, and
a controller that can be programmed to oversee assay preparation and analysis.

50. The system of claim 49, wherein the assay preparation unit includes a fluid dispensing system.

51. The system of claim 49, wherein the fluid dispensing system includes an array of dispense tips that are capable of non-contact dispensing of droplets of less than about 5 microliters per droplet.

52. The system of claim 51 further comprising a registration device capable of moving the array of dispense tips relative to the microplate so that the same array of dispense tips can be used to dispense fluid into microplates having different densities of wells.

53. The system of claim 49, wherein the assay preparation unit includes two microplate stacking stations, each of the stacking stations including a singulation mechanism that is capable of adding and subtracting a microplate to and from the bottom a microplate stack.

54. The system of claim 49, wherein the analyzer is programmed to receive information based on detection of a reference fiducial in the microplate.

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55. The system of claim 49, wherein each well in the microplate has a frusto-conical shape.

56. The system of claim 49, wherein the assay preparation unit includes an incubation chamber.

57. The system of claim 56 further comprising lid-spacing devices that separate 5 adjacent microplates in the incubation chamber.

58. The system of claim 50, wherein the assay preparation system includes a cycling mechanism that allows a microplate to be cycled automatically through the fluid dispensing station multiple times.